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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/644,664	08/20/2003	Viktor Kuvshinov	Kuvshinov 1-intron	3613

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John Dodds
1707 N St. NW
Washington, DC 20036

EXAMINER	
FOX, DAVID T	

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 05/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/644,664	KUVSHINOV ET AL.	
	Examiner	Art Unit	
	David T. Fox	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-42* is/are pending in the application.

4a) Of the above claim(s) *17-20 and 37-40* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16,21-36,41 and 42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *20 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *09 September 2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Applicant's election without traverse of Group II in the reply filed on 08 March 2006 is acknowledged. Upon further consideration, the Examiner has decided to rejoin Group I. Accordingly, claims 1-16, 21-36 and 41-42 are examined in the following Office action. Claims 17-20 and 37-40 are withdrawn as being drawn to non-elected inventions.

This application is a continuation-in-part of application no. 09/617,543 filed 14 July 2000, now U.S. Patent 6,849,776. The parent application disclosed the instantly claimed invention, namely the insertion of a blocking construct within an intron of the transgene of interest (see, e.g. the '776 patent, Figures 2A and 3; and Example 5, column 26, line 20 through column 27, line 30). Accordingly, the effective filing date for the instantly claimed subject matter is 14 July 2000.

The specification is objected to for the following informalities. All amendments should comply with 37 CFR 1.121(b).

On page 1, line 6, the issued patent number of the parent application should be inserted after the filing date of the parent application.

On page 1, line 9, "an" should be replaced with ---and---.

On page 10, line 6, "to" should be replaced with ---two---.

On pages 21-25, there are two Example 5's and no Example 8. The following amendments would obviate this aspect of the objection:

On page 23, line 19, replace "Example 5" with ---Example 6---.

On page 24, line 9, replace "Example 6" with ---Example 7---.

On page 25, line 4, replace "Example 7" with ---Example 8---.

On page 27, line 20, replace "I" with ---in---.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2-6, 9-12, 21-36 and 41-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Dependent claims are included in all rejections. All suggested claim amendments should comply with 37 CFR 1.121(c).

Claims 2-3 and 9-12 are indefinite in their recitation of "the RC" which lacks antecedent basis. Amendment of claim 1, penultimate line, to insert ---(RC)--- after "construct" would obviate this rejection.

Claims 4 and 24 are indefinite in their recitation of "wherein the BC is barnase and the RC is barstar" which is confusing, since the BC and RC are nucleotide constructs, while barnase and barstar are proteins.

Amendment of claims 4 and 24 to replace "is" with ---encodes---, all occurrences, would obviate this rejection.

Claims 5-6 are indefinite in their recitation of "nucleotide sequence SEQ ID NO:1 [or 2]" which is awkward. Insertion of ---comprising--- after "sequence" in line 2 of each claim would obviate this rejection.

Claim 21 is indefinite in its recitation of "the transgenic plant" which lacks antecedent basis. The following amendments would obviate this rejection:

In claim 21, line 4, replace "the" with ---a---.

In claim 21, line 5, insert ---containing said BC--- after "plant".

Claims 25-26 are indefinite in their recitation of "barnase [or barstar] comprises the SEQ ID NO:1 [or 2]" which is awkward and confusing, since a protein cannot comprise a nucleotide. The following claim amendments would obviate this rejection:

In claims 25-26, line 2, replace "comprises the" with ---is encoded by a nucleotide sequence comprising---.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-3, 7-16, 21-23, 27-36 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to nucleic acid molecules comprising any blocking construct and recovering construct of any sequence and from any gene, encoding any product of any sequence, including RNA or protein; said blocking and recovering constructs being inserted into any intron of any sequence; and plant cells and plants transformed therewith. In contrast, the specification only teaches blocking constructs which comprise a barnase protein-encoding region and recovering constructs comprising a barstar protein-encoding region.

The Federal Circuit has recently clarified the application of the written description requirement. The court stated that a written description of an invention "requires a

precise definition, such as by structure, formula, [or] chemical name, of the claimed subject matter sufficient to distinguish it from other materials." University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568; 43 USPQ2d 1398, 1406 (Fed. Cir. 1997). The court also concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id. Further, the court held that to adequately describe a claimed genus, Patent Owner must describe a representative number of the species of the claimed genus, and that one of skill in the art should be able to "visualize or recognize the identity of the members of the genus." Id.

Finally, the court held:

A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or a recitation of structural features common to members of the genus, which features constitute a substantial portion of the genus. Id.

See also MPEP Section 2163, page 174 of Chapter 2100 of the August 2005 version, column 1, bottom paragraph, where it is taught that

[T]he claimed invention as a whole may not be adequately described where an invention is described solely in terms of a method of its making coupled with its function and there is no described or art-recognized correlation or relationship between the structure of the invention and its function. A biomolecule sequence described only by a functional characteristic, without any known or disclosed correlation between that function and the structure of the sequence, normally is not a sufficient identifying characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence.

See also Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ 2d 1016 at 1021, (Fed. Cir. 1991) where it is taught that a gene (which includes a promoter) is not reduced to practice until the inventor can define it by "its physical or chemical properties" (e.g. a DNA sequence).

Given the claim breadth and lack of guidance as discussed above, the specification fails to provide an adequate written description of the genus of sequences as broadly claimed. Given the lack of written description of the claimed genus of sequences, any method of using them, such as transforming plant cells and plants therewith, and the resultant products including the claimed transformed plant cells and plants containing the genus of sequences, would also be inadequately described. Accordingly, one skilled in the art would not have recognized Applicant to have been in possession of the claimed invention at the time of filing. See the Written Description Requirement guidelines published in Federal Register/ Vol. 66, No. 4/ Friday January 5, 2001/ Notices: pp. 1099-1111.

Claims 1-16, 21-36 and 41-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for claims limited to a system comprising a blocking construct comprising a barnase coding sequence operably linked to an embryo- or germination- specific promoter, said blocking construct fully inserted within an intron of a transgene of interest; and a recovering construct comprising a barstar coding sequence operably linked to a physically inducible promoter; and plant cells and plants transformed therewith; does not reasonably provide enablement for claims broadly drawn to any blocking or recovering construct of any sequence encoding any product of any sequence, any blocking construct under the control of a constitutive promoter or other non-exemplified promoter type, any blocking construct which is only partially inserted into an intron of a transgene of interest, a recovery construct with any type of means for its expression control, and plant cells and plants transformed therewith. The specification does not enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Claims 1-3, 7-16, 21-23, 27-36 and 41-42 are broadly drawn to nucleic acid molecules comprising any blocking construct and recovering construct of any sequence and from any gene, encoding any product of any sequence, including RNA or protein; said blocking and recovering constructs being inserted into any intron of any sequence; and plant cells and plants transformed therewith. Claims 1-3, 7-12, 16, 21-23, 27-32, 36 and 41-42 are broadly drawn to blocking constructs with any type of promoter including constitutive promoters or promoters expressed in a variety of above-ground or below-ground plant parts at a variety of developmental stages. Claims 1-3, 7-8, 13-16, 21-23, 27-28, 33-36 and 41-42 are drawn to any means for controlling the expression of the recovery construct, including topical chemical application. Claims 1-16, 21-26 and 41-42 are broadly drawn to blocking constructs which are inserted either partially or fully into an intron of a transgene of interest.

In contrast, the specification only teaches blocking constructs which comprise a barnase protein-encoding region and recovering constructs comprising a barstar protein-encoding region, wherein the blocking construct has an embryo- or germination-specific promoter and the recovering construct has a heat shock- inducible promoter, and wherein the blocking construct is fully inserted into an intron of a transgene of interest. No guidance is provided for a multitude of non-exemplified blocking or recovering constructs with a multitude of non-exemplified coding or regulatory sequences. Furthermore, no guidance is provided for the partial insertion of a blocking

construct within an intron of a transgene of interest, wherein both the blocking construct and the transgene of interest would be fully functional.

The insertion of functional genes into introns, wherein the gene initially comprising the intron is also fully functional, is unpredictable. See, e.g., page 15 of the specification, lines 9-22 and page 16, lines 1-2; where it is taught that plant introns do not naturally comprise entire genes, that A-T content must be altered to conform with strict requirements for proper splicing, that introns are very short and would not be expected to tolerate large insertions, and that insertion of introns can decrease gene expression. Furthermore, it appears that partial insertion of the blocking construct into an intron of a transgene of interest would result in partial insertion of the blocking construct into an exon of the transgene of interest, thus altering the reading frame of the transgene of interest, and preventing or altering its expression.

The expression of a blocking construct encoding a lethal gene product is unpredictable, particularly under the control of non-exemplified promoters. The claimed blocking construct blocks development and/or reproduction of the plant, leading to plant death and/or sterility. If the blocking construct were expressed under the control of a constitutive promoter, lethal gene product would be expressed in all plant tissues at all plant development stages, and the plant would be killed before it could express the transgene of interest in sufficient quantities to obtain the desired protein product or phenotypic trait. Even if the blocking construct were expressed under the control of a tissue-specific promoter such as a photosynthesis-specific RUBISCO promoter, all above-ground plant parts would be affected, and the plant would die prematurely.

Similarly, if the blocking construct were expressed under the control of a root-specific promoter, the plant could be killed due to lack of ability to absorb water or nutrients, before the transgene of interest were sufficiently expressed.

See Kuvshinov et al (2004, Applicant submitted) on page 179, column 2, third paragraph, where it is taught that the use of unspecific promoters in the blocking construct resulted in premature fruit drop. Such an effect would not be desired if the transgene of interest were to be expressed in ripe fruit, in order to improve fruit quality. See also Daniell (2002, Applicant submitted) on page 582, Table 1 and page 585, column 1, first three paragraphs; where it is taught that few chemically-inducible promoters are commercially available or effectively penetrating, and that such promoters would not be useful for transgenes conferring traits which would be required throughout the life of the plant.

The use of non-exemplified treatments to activate the recovering constructs, such as topical chemical application, is unpredictable. See, e.g., Kriete et al, page 815, column 1, top paragraph; who teach non-target toxicity effects and failure of chemical persistence to produce desired effects in target tissues. See also Kuvshinov 2004, page 176, column 2, bottom paragraph, who teach the requirement for a heat shock-inducible promoter in the recovering construct.

Furthermore, the use of non-exemplified BC and RC coding sequences is unpredictable. See Williams, page 347, column 1, second and fourth paragraphs; page 348, Table 1; who teaches that only the barstar/barnase RC/BC system was successful

in both restoring fertility of both the targeted (male) tissues and avoiding adverse effects on other (female) tissues.

Given the claim breadth, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to identify and evaluate a multitude of non-exemplified blocking and recovering coding sequences for successful gene containment. Undue experimentation would have also been required to identify and evaluate a multitude of non-exemplified promoters for the blocking and recovering constructs, which promoters would successfully block transgene spread while simultaneously allowing effective transgene expression in the initially transformed plant. Furthermore, undue experimentation would have been required to develop methods for successful transgene expression into which a blocking construct was partially inserted into an exon of the transgene.

The claims are deemed free of the prior art, given the failure of the prior art to teach or reasonably suggest plant transformation with a system comprising a blocking construct embedded in an intron of another transgene of interest.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David T. Fox whose telephone number is 571-272-0795. The examiner can normally be reached on Monday through Friday from 10:30AM to 7:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anne Marie Grunberg, can be reached on 571-272-0975. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

May 26, 2006

DAVID T. FOX
PRIMARY EXAMINER
GROUP 1~~80~~ 1638